5 Fraser CG, Smith BC, Peake MJ. Effectiveness of an outpatient urine screening programme. *Clin Chem* 1977;**23**:2216-8.
6 Sorahan T, Parkes HG, Veys CA, Waterhouse JAH, Straughan JK, Nutt A. Mortality in the British rubber industry 1946-85. *Br J Ind Med* 1989;**46**:1-11.
7 Cartwright RA, Gadian T, Garland JB, Bernard SM. The influence of malignant cell cytology screening on the survival of industrial bladder cancer cases. *J Epidemiol Community Health* 1981;**35**:35-8.
8 Ellwein LB, Farrow GM. Urinary cytology screening: the decision facing the asymptomatic patient. *Med Decis Making* 1988;**8**:110-9.
9 Health and Safety Executive. *Control of substances hazardous to health. Approved code of practice. 29. Control of carcinogenic substances.* London: HMSO, 1988.
10 Wallace DMA. Occupational urothelial cancer. *Br J Urol* 1988;**61**:175-82.
11 Jacobs R. A review of the effectiveness of urinary cytology as a screening technique for occupational bladder cancer. *J Soc Occup Med* 1987;**37**:24-6.

# Endothelins

## *Chemical messengers with many functions*

Our understanding of the network of chemicals by which cells communicate with each other is becoming ever more detailed. The endothelins are the latest chemical messengers in a long line that began with insulin and thyroxin and has recently included the interleukins and the leukotrienes. Endothelins (like many other similar chemicals) were first recognised in a cell culture supernatant—in this case endothelial cells from the pig aorta.[1] The name endothelin was given to a peptide present in the culture fluid that caused the contraction of vascular strips—and did so with a greater potency than any known mammalian vasoconstrictor.

Information from a library of human recombinant DNA has shown that three distinct genes code for three endothelins.[2] Each of the three endothelins comprises 21 amino acid residues, and endothelin 2 and endothelin 3 differ from endothelin 1 in only two and five positions respectively. Endothelin 1 is derived from a 203 amino acid polypeptide, which is truncated to produce a 38 amino acid intermediate called "big" endothelin 1 before the final cleavage to the 21 amino acid active molecule.[3] So similar are the three endothelins that most antisera raised against one cross react with the other two, and for this reason it has been difficult to distinguish between their various localisations and activities. Nevertheless, they are thought to have different receptors and functions.

As with the interferons and the interleukins the cells from which endothelins were originally derived have proved to be only one of several production sites, and the activity first observed is not necessarily the most important. Cells capable of secreting endothelins may be identified by radioimmunoassay of cell culture supernatant; by immunocytochemical staining; or, most convincingly, by the recognition of specific messenger RNA by in situ hybridisation. With these techniques epithelial cells from the renal and respiratory tracts[4,5] and neurones of the spinal cord[6] have been suggested as sites of endothelin synthesis as well as the vascular endothelial cells in which they were first detected. Receptors for endothelin have been detected in the respiratory tract, and endothelins produce bronchoconstriction when inhaled or injected intravenously.[7,8] They also act as growth promoters and mitogens for various cell types, including Swiss 3T3 fibroblasts,[9] quiescent rat glomerular mesangial cells,[10] and rat vascular smooth muscle cells.[11]

From this welter of information can we say how important the endothelins are? Clearly they play some part in regulating vascular tone. Concentrations of messenger RNA encoding endothelin 1 increase rapidly on exposure to thrombin or adrenalin,[12] both of which are potent stimulators of platelet aggregation. This suggests that endothelins have an important role in haemostasis. Within the lung their bronchoconstrictor activity implies a role in asthma, but endothelin like immunoreactivity has also been localised to pulmonary endocrine cells, especially in the fetal lung,[5] and in non-small cell carcinomas of the lung.[13] It may be that the mitotic function operates in the embryological development of the lung and even that the growth promoting activity plays a part in the aetiology of pulmonary tumours.

Finally, endothelins may contribute to the degree of myocardial damage after coronary thrombosis. One study in rats showed that infusion of monoclonal antibody to endothelin reduced the area of infarction after ligation of the left coronary artery.[14]

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1 Yanagisawa M, Kurihara H, Kimura S, *et al.* A novel potent vasoconstrictor peptide produced by vascular endothelial cells. *Nature* 1988;**332**:411-5.
2 Inoue A, Yanagisawa M, Kimura S, *et al.* The human endothelin family: three structurally and pharmacologically distinct isopeptides predicted by three separate genes. *Proc Natl Acad Sci USA* 1989;**86**:2863-7.
3 Yanagisawa M, Masaki T. Molecular biology and biochemistry of the endothelins. *Trends in Pharmacological Sciences* 1989;**101**:374-8.
4 Kitamura K, Tanaka T, Kato J, Eto T, Tanaka K. Regional distribution of immunoreactive endothelin in porcine tissues: abundance in inner medulla of kidney. *Biochem Biophys Res Commun* 1989;**161**:348-52.
5 Rozengurt N, Springall DR, Polak JM. Localisation of endothelin-like immunoreactivity in airway epithelium of rats and mice. *J Pathol* 1990;**160**:5-8.
6 Giaid A, Gibson SJ, Ibrahim NBN, *et al.* Endothelin, an endothelium derived peptide is expressed in neurones of the human spinal cord and dorsal root ganglia. *Proc Natl Acad Sci USA* 1989;**86**:7634-8.
7 Power RF, Wharton J, Zhao Y, Bloom SR, Polak JM. Autoradiographic localisation of endothelin-1 binding sites in the cardiovascular and respiratory systems. *J Cardiovasc Pharmacol* 1989;**13**:550-6.
8 Turner NC, Power RF, Polak JM, Bloom SR, Dollery CT. Contraction of rat tracheal smooth muscle by endothelin. *Br J Pharmacol* 1989;**98**:361-6.
9 Takuwa N, Takuwa Y, Yanagisawa M, Yamashita K, Masaki T. A novel vasoactive peptide endothelin stimulates mitogenesis through inositol lipid turnover in Swiss 3T3 fibroblasts. *J Biol Chem* 1989;**264**:7856-61.
10 Simonson MS, Wann S, Mene P, *et al.* Endothelin stimulates phospholipase C, $Na^+/H^+$ exchange, c-fos expression, and mitogenesis in rat mesangial cells. *J Clin Invest* 1989;**83**:708-12.
11 Komuro I, Kurihara H, Sugiyama T, Takaku F, Yazaki Y. Endothelin stimulates c-fos and c-myc expression and proliferation of vascular smooth muscle cells. *FEBS Lett* 1988;**238**:249-52.
12 Gordon J. Vascular biology: put out to contract. *Nature* 1988;**332**:395-6.
13 Gaid A, Hamid QA, Springall DR, *et al.* Detection of endothelin immunoreactivity and mRNA in pulmonary tumours. *J Pathol* (in press).
14 Watanabe T, Suzuki N, Shimamoto N, Fujino M, Imada A. Endothelin in myocardial infarction. *Nature* 1990;**344**:114.

## Correction

### Emergency treatment of avulsed teeth

An author's error occurred in this editorial by Mr Barry Scheer (7 July, p 4). The concentration of chlorhexidine in the mouth rinse used to reduce accumulation of plaque should have been 0·2% and not 2% as published.